

these two amines in a qualitatively different fashion. It is thus possible that the type of interaction between these two amines and an analgesic might be a useful acute method of predicting whether or not the analgesic is narcotic in character.

AH 7921 and profadol were gifts from Allen & Hanburys, and Parke Davis & Co., respectively. Boehringer Sohn, Ingelheim, provided generous financial support.

REFERENCES

- BEAVER, W. T., WALLENSTEIN, S. L., HOUDE, R. W. & ROGERS, A. (1969). *Clin. Pharmac. Ther.*, **10**, 314-319.
 BRITAIN, R. T., KELLETT, D. N., NEAT, M. L. & STABLES, R. (1973). *Br. J. Pharmac.*, **49**, 158-159p.
 CALCUTT, C. R. & SPENCER, P. S. J. (1971). *Ibid.*, **41**, 401-402p.
 SEWELL, R. D. E. & SPENCER, P. S. J. (1974). *Ibid.*, **51**, 140-141p.
 SPARKES, C. G. & SPENCER, P. S. J. (1971). *Ibid.*, **42**, 230-241.

The binding of zinc to human serum proteins

T. J. BRADLEY AND H. SEN

Department of Pharmacy, The University, Manchester M13 9PL, U.K.

Zinc has been shown to be bound by the proteins in human serum with 2-8% being associated with low molecular weight components (Prasad & Oberleas, 1970). As previous work has been with ionic zinc, we have studied the binding of zinc from a zinc aminoacid complex.

^{65}Zn (L-Histidine) $_2$ 2H $_2$ O was prepared and volumes (0.1 to 2.0 ml) of a standard solution (1.75 mg Zn per ml and specific activity 34 μ Ci ml $^{-1}$) were mixed with constant volumes (5.0 ml) of pooled human serum and the mixture shaken at 37° for 30 min. The percentage of zinc associated with low molecular weight constituents of serum was found by separating the protein bound zinc in a "Millipore" hi-flux ultrafiltration cell having a "Pellicon" membrane of nominal molecular weight cut off 1000. The ultra-filtrate (0.1 ml) was examined for ^{65}Zn activity using a Harwell model 2000 well type scintillation counter. The activity in the ultrafiltrate was expressed as a percentage of the initial activity in the mixture prior to ultrafiltration.

The results were compared with those obtained using a standard solution of $^{65}\text{ZnCl}_2$ (1.75 mg Zn per ml and specific activity 135 μ Ci per ml) in similar experiments and shown in Fig. 1.

When the volume of $^{65}\text{ZnCl}_2$ solution added ranged from 0.1 ml to 1.0 ml the percentage of ^{65}Zn appearing in the ultrafiltrate was of the order of 2-3%. As the volume of $^{65}\text{ZnCl}_2$ solution was increased above 1.0 ml a sharp increase in the percentage of ^{65}Zn in the ultrafiltrate occurred until 9% appeared after 2.0 ml had been added. In the case of ^{65}Zn (L-His) $_2$ 2H $_2$ O the amount of ^{65}Zn appearing in the ultrafiltrate was greater by a factor of 10; from 10% for 0.1 ml of the standard solution added to 90% for 2.0 ml. Also the shape of the plot indicates that there is an exponential relationship between the amount of ^{65}Zn added and the amount of "free" zinc, i.e. zinc not bound by serum proteins.

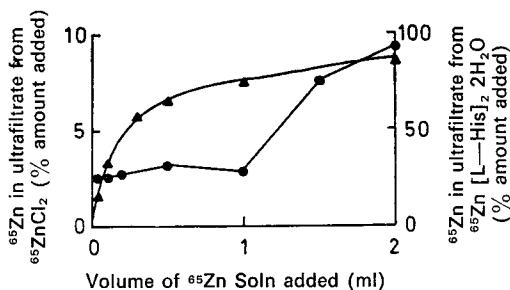


FIG. 1. The percent of ultrafiltrable ^{65}Zn plotted against the volume of ^{65}Zn solutions added. \blacktriangle — \blacktriangle — \blacktriangle Zn (His) $_2$ 2H $_2$ O: \bullet — \bullet — \bullet ZnCl $_2$.

The amount of ^{65}Zn associated with low molecular weight constituents in pooled human serum, *i.e.* the fraction of zinc in the circulation called 'free' zinc, may be increased by administering zinc in the form of zinc-histidine.

REFERENCE

PRASAD, A. S. & OBERLEAS, D. (1970). *J. Lab. clin. Med.*, **76**, 416-425.

The effect of blending on the physical properties of acid and alkaline gelatin gels

J. A. J. ROBINSON, I. W. KELLAWAY AND C. MARRIOTT

Pharmaceutics Research Unit, The University, Nottingham NG7 2RD, U.K.

The relation between rigidity and concentration of gelatin gels has been studied extensively by Ferry (1948). Similar studies with gelatins having widely differing molecular weights have been restricted to 5-73% gels. Ferry (1948) found that the rigidity of a 50:50 mixture of two gelatins was lower than the arithmetic mean of the rigidities of the individual samples.

The viscoelastic properties of mixtures of acid and alkaline gels have been determined in the linear region for the concentration range 1.5-3.5% w/v using non-destructive creep compliance tests. Rigidities of the mixtures have been measured using a modified Saunders and Ward rigidiometer, (Timson & Kelly 1966), for the concentration range 10-50%.

1.5-3.5% w/v gels were prepared and maintained at 50° for 1 h and then at 4° for 21 h. The gels having been equilibrated at 25° for 2 h were loaded between the cone and plate of an air turbine viscometer (Marriott, Irons & Harris, 1973) and equilibrated for a further period of 1 h at 25° in a saturated atmosphere. Gels in the higher concentration range (10-50%) were prepared and maintained at 50° for 1 h, poured into the rigidiometer tubes, allowed to cool to 4° and aged for 21 h. The gels were equilibrated at 25° for 30 min and rigidities determined.

The semi rigid gel mixtures (1.5-3.5% w/v) were opalescent and analysis of the creep compliance curves indicated a decrease in gel structure when compared with the unmixed gelatin gels. The 75:25 acid/alkaline gelatin mixture was found by 'u' tube viscometry and microelectrophoresis to be at the isoelectric point and produced gels exhibiting a maximum compliance.

Conversely, rigid gels (10-50% w/v) exhibited increases up to 15 fold over acid and alkaline samples upon mixing and broad maxima occurred in the rigidity-concentration graphs between 40-50% alkaline, 50-60% acid blends. Charge effects did not appear critical in the more rigid gel network resulting from the interaction between acid and alkaline samples. The increase in rigidity may be due to an increase in entanglements, interactions between end groups in both samples or incorporation of the lower molecular weight acid gelatin chains into the gel interstices of the higher molecular weight alkaline chains giving rise to a 'filling' effect.

REFERENCES

FERRY, J. D. (1948). *J. Am. chem. Soc.*, **70**, 2224.

MARRIOTT, C., IRONS, L. I. & HARRIS, E. R. (1973). *J. Phys. E: Sci. Instrum.*, **6**, 200-201.

TIMSON, W. J. & KELLY, W. D. (1966). *J. Photograph. Sci. Eng.*, **10**, 278-280.